Preliminary Comments
Chemical Assessment Advisory Committee Augmented for the Review of the EPA's Draft IRIS Benzo[a]pyrene Assessment

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1. **Literature search/study selection**. Is the literature search strategy well documented? Please identify additional peer-reviewed studies that might have been missed.

The report cites the absorption-from-soil literature uncritically. At a minimum, arguments in Spalt et al. (2009) and Kissel (2011) should be considered.

Spalt EW, JC Kissel, JH Shirai, AL Bunge. 2009. Dermal absorption of environmental contaminants from soil and sediment: A critical review. *J Expos Sci Environ Epid.* 19:119-148.
Kissel JC. 2011. The mismeasure of dermal absorption. *J Expos Sci Environ Epid.* 21(3):302-9.

5. **In August 2013, EPA asked for public comments** on an earlier draft of this assessment. Appendix G summarizes the public comments and this assessment's responses to them. Please comment on EPA's responses to the scientific issues raised in the public comments.

I will confine my preliminary comments to the question of "Real World" validation of the dermal slope factor as this appears to be a key point of contention.

Comments submitted on behalf of the American Coke and Coal Chemicals Institute and others in 2013 include the following statement:

> "USEPA (2013) has not performed even the most cursory real world validation of the proposed DSF to see if it makes any logical sense."

The public comment document then offers brief analyses that purport to find that EPA's analysis leads to untenable outcomes (i.e., over-prediction of skin cancer in the general population and in psoriasis patients treated with coal tar ointments). This argument was essentially repeated in the March teleconference.

EPA's response on these points is very brief and inadequate. Certainly it is reasonable to ask whether the proposed slope factor would lead to predictions that are clearly implausible. EPA declares that it cannot evaluate the public comments on the grounds that full details were not provided. However, I was able to reproduce the claims presented in the public comments (which evolved slightly between 2013 and 2015), at least in general terms, with relatively little effort.

Soil Contact. Prediction, in public comments, of high risk of skin cancer in the general populace due to soil contact is based partly on EPA arguments and partly on amendment of those arguments with additional assumptions. EPA's base case (found in Appendix G of the Supplemental Material) is described as a Central Tendency Estimate (CTE). Persons familiar with EPA practices understand that a CTE is an imprecisely defined estimate. EPA's Exposure Factors Handbook defines CTE as:

> *Central tendency exposure—A measure of the middle or the center of an exposure distribution. The mean is the most commonly used measure of central tendency.*

In practice, since actual parameter distributions are not known, individual parameter values may be medians, means or some other statistic. When multiplied together, the results tend to be conservative, but to an unknown degree (and occasionally not at all). EPA continues to move slowly toward probabilistic approaches (a new document released by EPA's Risk Assessment Forum in 2014 states that it intends to encourage such action), but routinely reverts to deterministic approaches in cases such as this.

In the Appendix G scenario, for instance, EPA assumes all individuals contact outdoor soil or housedust indistinguishable from soil clothed in shorts and T-shirts 350 days per year for 18 years. Since the early 1990's the regulated community has complained that EPA's risk assessments suffer from "compounded conservatism," i.e., multiplication of individually conservative assumptions that in aggregate produce an outcome that represents an extreme upper tail of the population. Nevertheless, the public commenters extend that string of 350 shorts-and-T-shirts-days per year to 70 consecutive years. In concert with other assumptions unlikely to be underestimates, the public commenters produce a point estimate of risk, which they then apply to the whole population. Since that point estimate actually applies at some unspecified population fractile, it is not reasonable to assume that it applies to the whole population. EPA would be in a better position to respond if they had conducted a probabilistic assessment. This issue requires further attention from the committee.

Coal Tar Ointment Contact. The public commenters' argument is based on failure to observe elevated skin cancer in persons undergoing pharmaceutical treatment for skin disease. However, psoriasis patients are unlikely to be a relevant comparison population. Chapman et al. (1979) and Shuster et al. (1980) have found reduced AHH activity in psoriasis patients and suggested that they may be genetically less susceptible to PAH-induced carcinogenicity as a result. In addition, psoriasis patients are known to shed skin cells at greatly elevated rates (Weinstein & McCullough, 1973). Desquamation can reduce penetration beyond the stratum corneum of compounds, such as PAHs, that are lipophilic

and sorb to skin cells (Reddy et al., 2000). Both mechanisms could be protective with respect to skin cancer risk due to external contact with PAHs. The finding by Roelofzen et al. (2012) of reduced 1-hydroxypyrene in urine and PAH-DNA adducts in biopsied skin in psoriasis patients in comparison to healthy volunteers following dosing with coal tar ointments is consistent with this logic. EPA discounts the pharmacological use cases due to poor quantitation of actual exposures, but fails to note that the population involved is an inherently poor surrogate for the general populace.